**Annual Review of Neuroscience, 2015.** Steven E. Hyman, Thomas M. Jessell, Carla J. Shatz and Huda Y. Zoghbi (eds). Annual Reviews, 4139 El Camino Way, PO Box 10139, Palo Alto, California 94303-0139, USA. Vol. 38. ix + 468 pages. Price: US$ 99.

The *Annual Review of Neuroscience* presents a collection of topical reviews covering all sub-areas of neuroscience. This volume contains 21 reviews, spanning fundamental neuroscience and translational research.

In the last quarter of the previous century, simple organisms with relatively few neurons offered hope for cracking circuits[1]. Neuroscience research in the post-genomic era is no longer shying away from the astronomical numbers of genes, synapses or neurons. I describe here a few of the relevant reviews from this volume that describe how genomic, genetic and physiological data coming from humans and animal models can help us better understand the brain in health and disease.

Our ability to see the world around us is made possible by complex neural circuits in the eye and the brain. Whatever the brain knows about the visual world, it knows via the action potentials fired by retinal ganglion cells (RGCs). RGCs are not just simple luminance detectors, but have interesting spatial and temporal receptive field properties. Prominent features of the visual world such as edges, directional movement and luminance contrast can be detected by RGCs. Thus, instead of simply conveying pixel-by-pixel light intensity to the brain like a camera, RGCs are feature detectors that send parallel channels of features of the visual world to the brain. This is made possible by the diverse types of RGCs, each of which is specialized to detect a feature of the visual input. In an edifying review, Joshua Sanes and Richard Masland, describe the known types of RGCs and the kinds of computation they can perform. They count a total of about 30 types of RGCs based on response types, morphology, marker expression and laminar position. These 30 classes together account for more than 95% of RGCs, and the classification map provided in the review is immensely useful for retinal physiologists. But more importantly, this exercise in classifying RGCs offers new insights and lessons for the immensely more difficult task of classifying and grouping neurons in the brain, such as cortical pyramidal neurons. Some of the points to remember are: (1) It is better to use a combination of molecular markers instead of single gene markers to identify neurons. (2) Cells expressing the same molecular markers may exhibit different electrical activity, plasticity or morphology, and therefore classification with each of these parameters may yield different results. (3) Cell classes may be conserved across species, if they perform similar functions. (4) Different cell types may make different patterns of synaptic connections during development and may respond differently to injury or insults later in life.

Synaptic connections between neurons are constantly regulated to make them weaker or stronger depending on patterns of activity in the circuit. In 1949 Hebb[2] postulated that neurons which fire together wire together. Excitatory synapses enable action potential firing, while inhibitory synapses suppress firing. To keep neural responses within the operating range, neurons must achieve a balance between excitatory and inhibitory synaptic strengths. Otherwise, they will either be constantly on or constantly off. A lot is known about how excitatory synaptic strength is regulated by neural activity in accordance with Hebb's postulate. Yet, comparatively less is known in this regard for inhibitory synapses. Robert Froemke reviews this vast literature focusing on known mechanisms by which excitatory and inhibitory synapses are regulated over the short and long terms. In short-term synaptic plasticity, changes of synaptic strength last only over several milliseconds to seconds. These changes could be in the probability of transmitter release (either facilitation or depression), or in the gating properties of post-synaptic receptor channels. In long-term plasticity, such as long-term potentiation (LTP) and long-term depression (LTD), long-lasting changes such as changes in the number of synaptic connections, number of receptor channels on the post-synapse, etc. are maintained over several minutes to hours, making LTP and LTD ideal candidates for the acquisition and storage of memories. To maintain neurons within their normal operating firing rates, whenever excitatory synaptic strengths are altered, inhibitory synaptic strengths also need to be altered. This is called maintenance of balance of excitation to inhibition. One of the mechanisms by which this balance is generated during development is by scaling the numbers of inhibitory synapses with newly forming excitatory synapses. Sensory experience also drives these processes, such that the balance is set at a level where neural firing can effectively code for sensory inputs. In addition, neuromodulators such as acetylcholine, noradrenaline and oxytocin can also shape balance between excitation and inhibition.

Synapses that use glutamate as the neurotransmitter (glutamatergic) are the most abundant in the central nervous system. Richard Huganir and co-workers review the known members of a glutamatergic synapse, and how they participate in its development and plasticity. They then proceed to document known mutations of proteins that are involved in glutamatergic synapse function. The availability of human genome data coupled with next-generation sequencing (NGS) of patient samples has made it possible to compile lists of genes with single nucleotide polymorphisms, copy number variations or mutations associated with neurological disease. Huganir and co-workers focus on three neurological disorders not associated with old age: intellectual disability (ID), autism spectrum disorders (ASD) and schizophrenia (SCZ). They report that disease-associated genetic variations occur at loci that code for not only those proteins that are located at the synapse such as glutamatergic receptors, scaffold molecules and vesicle proteins, but also a wide array of proteins that function as transcription factors, translation suppressors and regulators of protein trafficking and turnover. Proteins that are involved in glycosylation pathways are also implicated in neurological diseases such as epilepsy, ID and ASDs, as described by Freeze *et al.* Proper glycosylation of target proteins is required for neural migration, synaptogenesis and plasticity. When key members of a glycosylation pathway are mutated, one or more of these processes are affected leading to abnormal function. Many of the candidate proteins identified are implicated in multiple disease conditions – glutamatergic receptors (both NMDARs and AMPARs), scaffold proteins like Homer and Shank, the neuroligin/neurexin synaptic adhesion complex and the synaptic translation

repressor FMRP are implicated in ID, ASD and SCZ as discussed by Huganir and co-workers. On the other hand, each disease condition is mapped onto mutations at multiple sites. For SCZ, a recent genome-wide association study (GWAS) of ~35,000 patients and ~100,000 control subjects identified about 600 candidate genes. Similarly, FMRP interacts with about 800 different mRNAs and it will be a herculean task to understand how any given FMRP mutation affects translation levels of each of these target mRNAs. In many cases, these data are corroborated by mutations of specific genes in mice. For example, mice lacking neurexins or neuroligins show ASD-related abnormal behaviours and deficits in glutamatergic synaptic transmission. Genomic data implicate the activity-regulated gene *Arc* in SCZ, and mice lacking *Arc* suffer deficits in memory consolidation. Thus, animal models can be utilized to better understand the functional readouts of genetic mutations identified in patients. An alternative approach is to derive neurons from human-induced pluripotent stem cells (hiPSCs) from patients and control subjects to understand how the mutation affects neural function. However, caution needs to be exercised with this approach for several reasons. These are pointed out by Heinzen and co-workers in their review of the genetics of neuropsychiatric diseases, as well as Huganir and co-workers. First, the penetrance of genetic mutations in causing the disease goes in the order ID > ASD > SCZ, while the influence of environmental factors to disease presentation goes in the order SCZ > ASD > ID. Secondly, these disorders are associated with low fecundity and the mutations rarely spread to high levels in the population to be detected via GWAS linkages. NGS of exomes is more powerful at detecting these rare variations and is being utilized. Thirdly, frequently, the disease is brought about by *de novo* mutations in the patient and is not detected in the parents. Even in the patient, if the mutation occurs at a later stage in development, leukocytes from which hiPSCs are derived may not harbour the mutation, while nervous tissue might. In these cases, deriving iPSCs from ectodermal tissue such as skin might be more fruitful. Fourthly, genetic variation associated with these diseases might occur outside of protein-coding regions and sequencing the exome will not reveal these variations. Lastly, gene discovery using GWAS and exome sequencing will yield a long list of contributing genes. To understand why these result in ID, ASD or SCZ, ingenious high-throughput functional assays are to be devised. The latest optogenetic neural stimulation and inactivation techniques together with imaging technologies offer hope in this regard.

1. Marder, E., *Nature*, 2002, **417**, 318–321.
2. Hebb, D., *The Organization of Behavior*, Wiley and Sons, New York, 1949.

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The present volume of the *Annual Review of Phytopathology* critically examines the developments in different aspects of plant diseases in a holistic manner through 28 comprehensive, well-illustrated and appropriately referenced reviews.

The opening chapter deals with the lifetime achievements of Dennis Gonsalves, who has made an indelible mark in the annals of phytopathology through his contributions spanning detection and characterization of papaya ring spot virus, cross-protection strategy and entry into molecular virology, culminating in a team approach for genetic engineering using pathogen-derived resistance (coat protein gene) approach for the development of transgenic papaya resistant to ring spot. The outcome of this research has helped to save the Hawaiian papaya industry from devastation by ring spot virus, marking the beginning of development of similar papaya for other countries. Certainly, this review is a source of inspiration alongside the human touch in a truly Hawaiian spirit of '*aloha*' to youngsters stepping into the field of plant pathology.

Precise identity of the pathogens is a basic requirement equally important for research, inspection, quarantine services and for sustainable disease management. Bacterial taxonomy has met with frequent changes due to insufficient knowledge of the pathogens, gained at diagnostic levels. Bull and Koike point out the dependability of molecular tools, over the phenotypic characteristics, particularly for diagnosing bacterial diseases. They stress that it is crucial to have accessibility to the use of modern molecular tools, including technologies based on multi-locus and whole-genome sequence analysis accompanied by hands-on-training to diagnostic technicians and pathologists directly in contact with extension workers and farmers at the diagnostic centres. However, these are applied now for already known pathogens and not for pathogen discovery. While pointing out the accelerated developments in fungal systematics in the recent decade and a half, which now incorporates genomics, web-based systems and DNA data enabling global collaborations for rapid identification of species to metadata, Crows *et al*. suggest linking names to type specimens, cultures and reference sequences. Use of DNA barcoding, progress made in attempts to merge sexual and asexual generic and species names for implementing one fungus–one name system and sequence-based classification of fungi, which will shed more light on fungal diversity are critically discussed. Presently, use of meta genomic approach employing the next-generation sequencing technologies aided by bioinformatics tools for the detection and identification of both known and new viruses and viroids infecting plants has gained momentum. Wu *et al*. bring to light the need for development of new computational algorithms capable of discovering novel viruses from next-generation sequencing datasets in a homology-independent manner, easily accessible user-friendly software interfaces and fulfilling Koch's postulates for the viruses and viroids.

Ever since Janeway's[1] concept of innate immunity was adopted to plant science[2], there has been an explosion in studies related to it during the past